Structure

In This Issue

In Review: Neurotransmitter Transporters

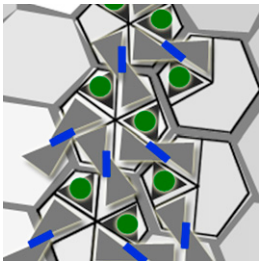
PAGE 694

In the central nervous system, sodium-coupled transporters function to remove neurotransmitters from the synaptic cleft. Focke et al. review structures, functional data, and simulations of neurotransmitter transporters and propose a mechanism for coupling sodium and substrate binding to conformational changes.

In Control of T Cells

PAGE 707

T cell activity is controlled by several distinct interactions including those arising from members of the B7 protein family. Vigdorovich et al. report the crystal structure of murine B7-H3, which provides a model for the organization of the IgV and IgC domains within the ectodomain.



Viral Ancient History

PAGE 718

Rissanen et al. propose a model for the architecture and assembly of bacteriophage P23-77 that is quite different from those previously published. The capsid proteins and their mode of association to form the virus particle suggest that P23-77 share a common evolutionary origin with the PRD1/Adenovirus lineage.

Mixed-Linkage, Mixed Messages

PAGE 727

The outcomes of linkage mixing in polyubiquitin are poorly understood. Nakasone et al. show that Lys48 and Lys63 linkages retain their distinctive structural and signaling properties in mixed-linkage branched and unbranched chains, suggesting a possibility of encoding multiple signals in the same polyubiquitin chain.

Going BIg

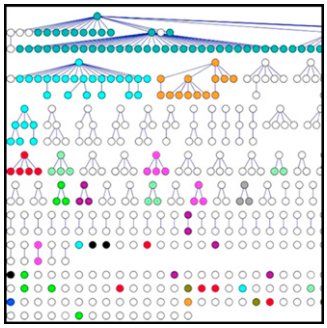
PAGE 741

Griessl et al. describe a structure for the 53 BIg domains of the giant adhesin SiiE from *Salmonella enterica*. They suggest a Ca^{2+}-rigidified 200 nm rod-like habitus for SiiE. Functional evidence links Ca^{2+} binding to pathogenicity, and the structure supports multiple routes for SiiE-bridged pathogen host interactions.

Rpt6 Helix-Coil Transitions

PAGE 753

Ehlinger et al. report that the C-terminal domain of proteasome ATPase Rpt6 undergoes dynamic helix-coil transitions, nucleated at helix-destabilizing glycines. Based on the analysis, they propose that Rpt6 dynamics plays an important role in proteasome assembly and expulsion of proteasome assembly chaperone Rpn14.



Brotherhood of Immune Regulatory Proteins

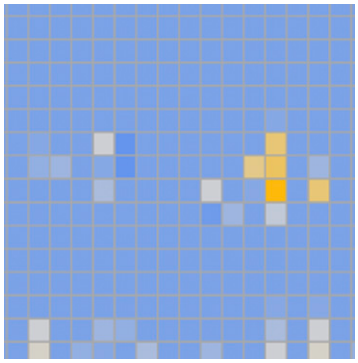
PAGE 766

Rubinstein et al. introduce a computational method (Brotherhood) that classifies proteins into functional families. The algorithm identified CRTAM as a new member of the nectin-like family, which was verified by the crystal structure. This also allowed identification of previously unknown homophilic interaction.

Structure of TatC

PAGE 777

The integral membrane protein TatC is the part of the twin-arginine translocation pathway that binds the signal sequence of folded proteins to initiate their secretion. Ramasamy et al. report a structure of TatC, which contains a binding pocket deep in the lipid bilayer, providing insight into the early translocation.



Looking at the Interaction Patterns

PAGE 789

The ability to predict the structures of various protein/protein complexes is critical for developing a systems view of cellular function. Verschueren et al. develop a method for de novo prediction of protein/peptide complexes and show that it also performs domain interaction site discovery and domain-domain docking.

Structure of Sphingosine Kinase 1

PAGE 798

Sphingosine kinase 1 (SphK1) is a lipid kinase that is central in modulating the S1P levels in cells. Wang et al. describe structures of human SphK1 that together with mutagenesis and kinetic studies, reveal how SphK1 recognizes the lipid substrate, catalyzes ATP-dependent phosphorylation, and permits inhibitor binding.

Lipid Interactions with Aquaporins

PAGE 810

Multiscale MD simulations developed by Stansfeld et al. allow prediction of the interactions of lipids with membrane proteins, illustrated here through aquaporins. The results of the simulations are in good agreement with available crystal structures and reveal a broadly conserved protein/lipid interface.

Talking to the Microbiome

PAGE 820

Hatherley et al. present a structural basis for why the cell surface protein CD200 binds to its receptor (CD200R) but not to the related activating receptor CD200RLa. The rapid evolution of the receptors was probably driven by pathogens and might play a role in mediating interaction with the microbiome.

Microtubule Stabilization by GTP

PAGE 833

Microtubules are dynamic constituents of the cell cytoskeleton. They grow with GTP and shrink with GDP. Quiniou et al. describe a mechanism by which GTP stabilizes microtubules through the combination of computational and cryo-ET work. Both curving and twisting of protofilaments during depolymerization plays a role.

Wzi's Role in *E. coli* capsule assembly

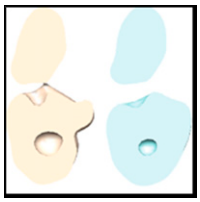
PAGE 844

Wzi is a novel β barrel outer membrane protein that is found in bacteria that make group 1 capsules. When the protein is missing or specific regions are mutated, capsule formation is impaired. Bushell et al. show that the protein binds to K30 capsular polysaccharide and suggest it templates capsule assembly.

ABC of Maintaining Vision

PAGE 854

The ABCA subfamily contains the largest and most complex ABC transporters but lacks structural information. Tsybovsky et al. use single-particle analysis and hydrogen/deuterium exchange to reveal the architecture and nucleotide-driven conformational changes of ABCA4, an ABCA member involved in maintaining vision.



Opening the Lid on an ABC Transporter

PAGE 861

S-components are small integral membrane proteins that bind transported substrates in ECF-type ABC transporters. Majsnerowska et al. show that binding of thiamin to the S-components ThiT requires the opening of a lid-like loop that occludes the binding site, with transmembrane helices forming a rigid scaffold.

